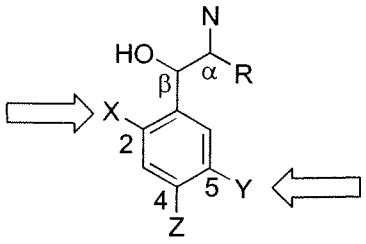
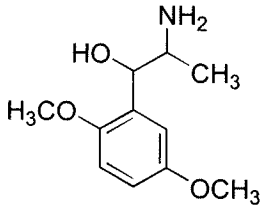
REMARKS

Claims 1-13 are currently pending in the application. No amendments are currently being made to the claims. The foregoing separate sheets marked as "Listing of Claims" show all the claims in the application, with an indication of the current status of each.

With respect to the compounds described in the references cited by the Examiner, there are some superficial structural similarities to the compounds of the present invention that could appear, to the untrained eye, to look important. Scientifically, they aren't. What is important for the pharmacological action of the compounds described in the present application is an **OH or small alkoxy group** at the 2- AND 5-positions. So, any compound that does not include these is irrelevant. Methoxamine (shown below) is a structurally related agent that possesses the 2, 5-dimethoxy substituents so, upon cursory inspection, it looks similar to the compounds of the invention. Methoxamine is a well known adrenergic agent with no known serotonergic actions.



Compounds of the present invention



Methoxamine

Another feature important for our compounds is a substituent at the 4-position (e.g. halogen, trifluoromethyl, or small alkyl such as Me, Et or Pr). The presence of this substituent converts methoxamine-like adrenergic agents to serotonergic agents – specifically, 5-HT_2 serotonin receptor agonists.

Claim Rejections: 35 USC § 103(a)

Claims1-13 stand rejected under 35 USC § 103(a) as obvious over Furukawa et al. (US 7,216,231, hereinafter "Furukawa"), Buschmann et al (US 6,344,558, herein after

"Buschmann"), Shell et al., Chiou et al, and/or Bodor et al. (hereinafter "Shell", Chiou" and "Bodor"). These rejections are traversed.

Applicant notes that Examiner, in making this rejection, has not precisely specified how 35 USC § 103(a) is being applied, other than that, with respect to the Furukawa reference, the Examiner (incorrectly) states that the replacement of methyl with H is "normally" considered obvious. With respect to Buschmann, Shell, Chiou and Bodor, the Examiner merely states that they teach "analogous" compounds, without defining "analogous", without providing an explanation of the differences between these references and the present invention, without any reference to specific combinations of these references, and, in short, without providing a rationale for an obviousness rejection. Applicant shows below that each reference does not render the present invention obvious, either alone or in combination with any other reference, because the compounds taught therein differ substantially from those of the present invention in non-obvious ways. No particular combinations of references were presented in the Office Action. Thus, the Examiner has failed to present a prima facie case of obviousness.

The claimed compounds and methods for using the compounds to treat glaucoma. The compounds contain two chiral centers, denoted α and β in formula I above. The α chiral center is created by the presence of CH_3 (instead of H) as a substituent of the carbon described by the Examiner as the "carbon adjacent to the nitrogen moiety". As a result, the compounds of the invention exist as four optical isomers. In contrast, the compounds described by Furukawa have only one chiral center. The single chiral center is located at the position analogous to that of the "β" chiral center in the compounds of the present invention (see formula I above). The compounds of Furukawa thus exist as only two optical isomers. In fact, Furukawa is directed to production of one or the other of these two isomers, i.e. to the production of a substantially pure enantiomeric optically active compound (see, for example, the abstract; the first sentence of the Summary in column 3 at lines 21-23; column 18, lines 6-32; the Examples, which describe the production of optically active compounds; and claim 1, which recites "A process for producing an optically active ...derivative..."). Whereas the compounds of the present invention require two chiral centers, creation of a second chiral center in the compounds of Furukawa would

nullify and render inoperative and/or destroy the invention of Furukawa, which *requires* the production of optically active compounds with a single chiral center. The methods of Furukawa could not be used to produce the compounds of the present invention and no straightforward or obvious variation of Furukawa's methods could be used to do so.

Examiner states that "the replacement of methyl with a hydrogen atom on [a] linking chain is normally within the sphere of obviousness that surrounds a known compound" and cites in re Wood 199 USPQ 137. Applicant has reviewed in re Wood. There is no 'linking chain" in the case. Rather, the controversy in the case concerned unsubstituted vs substituted 7,7' positions of a pyrazine *ring* (in particular, a gem dialkyl substitution in a saturated ring at the 7,7 position). Such a structure bears no similarity whatsoever to the ethylamine chain extending from the phenyl ring in the compounds of the present invention, and one of skill in the art would not consider that pyrazine chemistry could be correctly applied to the compounds currently under consideration.

In addition, Examiner appears to have treated to all claims of the present invention as composition claims, which they are not. Claims 1-8 are directed to a *method of treating glaucoma* using the compounds of the invention. The treatment of glaucoma is neither discussed nor alluded to by Furukawa. Rather, the compounds described by Furukawa are anti-obesity compounds. Applicant submits that one of skill in the art would not assume or find obvious the use of an anti-obesity agent to treat glaucoma. Thus, in addition to the significant differences between the compounds of the invention and those of Furukawa described above, method claims 1-8 of the present application are not rendered obvious in view of Furukawa in view of in re Woods.

With respect to Buschmann, the Examiner refers to the compounds disclosed therein as "analogous" without further describing the relevance of this reference to the claims of the present application. In fact, Buschmann has no bearing whatsoever on the present invention. Strikingly, the compounds disclosed by Buschmann have an additional methylene group in the chain that links the nitrogen to the phenyl ring, i.e. the Buschmann compounds are 1-phenyl-3-propylamines whereas those of the present invention are 1-phenyl-3-ethylamines. Those of skill

in the art would recognize that chain extension by as little as one atom *can* alter pharmacological action, and would not find the compounds or the action of the compounds of the present invention obvious in view of Buschmann. For example, 1-phenyl-3-propylamines (and compounds with longer side chains) are common adrenergic agents but not 5-HT_2 (serotonin) agents. In contrast, the compounds of the present invention are 5-HT_2 agonists (see first sentence of Summary). In addition, the compounds taught by Buschmann contain only two variable non-hydrogen substituents on the phenyl ring, R4 and R5, whereas the compounds of the present invention *require* three non-H substituents in the phenyl ring. In fact, in some embodiments of Buschmann, R5 is H so there is only one non-H substituent (see column 2, lines 21-29). One of skill in the art would recognize that such variations in substituent numbers would have consequences that were neither predictable nor obvious, and that the compounds of the present invention are not obvious in view of Buschmann.

In addition, Applicant reiterates that the claims of the invention are not directly exclusively to compounds but to methods of their use to treat glaucoma. This is a completely novel and non-obvious use in view of Buschmann, who describes only the treatment of pain. Applicant submits that one of skill in the art would not assume or find obvious the use of analgesics to treat glaucoma. Thus, in addition to the significant structural differences between the compounds of the invention and those of Buschmann, method claims 1-8 of the present application are not rendered obvious in view of Buschmann.

The Examiner refers to Shell, Chiou and Bodor as also teaching "analogous" compounds for treating glaucoma. This is also incorrect. For example, the compounds of the present invention have a *required* R^2 group (see formula I above) such that R^2 = C_{1-3} alkyl, Cl, Br, or I (with the proviso that when X = OH, R^2 is not I or methyl). The equivalent position of Shell, Chiou and Bodor is only H. One of skill in the art will recognize that the replacement of an H in a phenyl ring by substitutents such as C_{1-3} alkyl, Cl, Br, or I may greatly alter the properties of compounds containing in phenyl ring in non-predictable, non-obvious ways. Basically Shell, Chiou and Bodor teach analogs of methoxamine, a recognized adrenergic agent, and these compounds are adrenergic agents (see abstracts). In contrast, the compounds of the invention,

due at least in part to the presence of the non-H substituent at the R^2 group, are not adrenergic agents but rather 5-HT_2 agonists, as described above.

In summary, the compounds described by Furukawa, Buschmann, Shell, Chiou and Bodor all differ substantially and non-obviously from those of the present invention in structure, and knowledge of the structure of the compounds taught in these references, either individually or in any combination, would not render obvious the compounds of the invention. Further, the compounds described in each reference differ substantially form one another so that the properties of any one reference (e.g. of Shell, Chiou or Bodor for treating glaucoma) could not be obviously claimed to apply to the others (e.g. Furukawa or Buschmann) or to the non-obvious compounds of the present invention. Thus, the anti-glaucoma activity and 5-HT_2 properties of the compounds of the present invention are not obvious in view of any of the cited references, or in view of any combination of the cited references.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of this rejection.

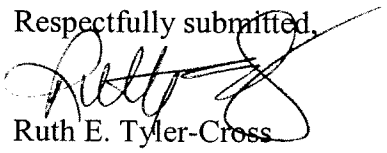
Concluding Remarks

In view of the foregoing, it is requested that the application be reconsidered, that claims 1-13 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: ruth@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

If an extension of time is required for this response to be considered as being timely filed, a conditional petition is hereby made for such extension of time. Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,



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